

## **REMARKS**

Claims 1-5, 50, 52, 54-56, 58 and 60 are under consideration in the instant application. To expedite the prosecution of commercially relevant subject matter, Applicants have herein canceled claims 1-5, 52, 56, and 58, and amended claims 50 and 60. The cancellations and amendments are not in acquiescence of any rejection, and Applicants reserve the right to pursue the same or similar subject matter in related applications. Accordingly, claims 50, 54, 55, and 60 are currently pending. Applicants have addressed the Examiner's concerns below in the order presented in the outstanding Office Action.

### **Rejections Under 35 U.S.C. § 112, First Paragraph, for Lack of Enablement**

Claims 50, 54, 55, and 60 stand rejected for allegedly containing subject matter which is not described in the specification in such as way as to enable one skilled in the art to make and/or use the invention. The claims have herein been amended to recite methods for delivering one or more substances, wherein the substance(s) comprise a polypeptide and/or substance(s) that preferentially bind to a polypeptide, and wherein the methods comprise the steps of providing vault-like particles comprising the polypeptide linked to a vault protein (MVP, VPARP, a portion of VPARP, or modified forms thereof), and administering the vault-like particles. Applicants submit that the amended claims are fully enabled by the specification, and, to the extent the enablement rejection is maintained over the amended claims, respectfully traverse.

The test of enablement is whether one reasonably skilled in the art could make or use the *claimed* invention from the disclosures in the patent coupled with information known in the art without undue experimentation. MPEP § 2164.01. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the scope of the claim, then the enablement requirement is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Moreover, the Examiner bears the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). A "disclosure which contains a

teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement ..., unless there is a reason to doubt the objective truth of the statements contained therein.” MPEP § 2164.04.

Applicants respectfully submit that the instant specification, in light of the knowledge in the art, teaches how to make and use the full scope of the claimed invention. For example, the instant specification describes a variety of vault-like particles and their component vault proteins (e.g., p. 8, lines 3-21). The specification also describes numerous modified forms of vault proteins, including MVP, VPARP, and portions of VPARP, that have non-vault polypeptides linked to their N-terminal and/or C-terminal ends, where the non-vault polypeptides comprise an active substance and/or bind one or more active substances (e.g., Specification, p. 8, lines 22-30 and pp. 11-19). The specification further describes methods for making the claimed vault-like particles using, e.g., a baculovirus expression system (e.g., Specification, p. 22, line 21 to p. 23, line 4), and general routes and dosages for administering vault-like particles (e.g., Specification, p. 9, lines 5-24). Since “a patent need not teach, and preferably omits, what is well known in the art,” (MPEP § 2164.01), and as acknowledged by the Examiner, “the level of skill in the art is high” (Office Action, p. 4), Applicants submit that the above teachings and the specification as a whole would have sufficiently enabled a skilled artisan to carry out the claimed invention without undue experimentation.

In support of the enablement rejection, the Examiner cites several factors set forth in *In re Wands* as evidence that undue experimentation would be required to carry out the claimed methods. Applicants have addressed several of the factors asserted by the Examiner below:

1) Unpredictability in the art - The examiner asserts that “the function of vaults, the molecules transported in, or by, vaults, the composition of vaults ..., [and] the function of the vault RNAs ... are poorly known or entirely unknown,” and that “recent research calls into

question the role(s) vaults may play in intracellular transport” (Office Action, p. 3). While these assertions may be relevant to the physiological role of vaults, questions of enablement are evaluated against the *claimed* subject matter (M.P.E.P. § 2164.01). Applicants submit that knowledge as to the physiological composition or role of vaults above that disclosed in the instant specification is not necessary to make and use vault-like particles according to the claimed methods.

2) State of the art - The Examiner asserts that “[t]he state of the art with regard to recombinantly engineering vaults to transport and deliver substances to target cells or tissues is nil” (Office Action, p. 3). Since the Examiner has acknowledged that “the claimed invention is free of the art” (Office Action, p. 5), one would not expect the claimed methods to be entirely within the state of the art. However, when considered in light of the teachings of the instant specification, the state of the art supports rather than opposes the enablement of the instant claims. As described above, the specification teaches, e.g., the components of the claimed vault-like particles as well as fusion constructs for carrying substances in such vault-like particles. In light of these teachings, Applicants submit that the advanced state of the art in molecular biology, pharmacology, and other relevant arts would enable a skilled artisan to make the claimed vault-like particles using standard recombinant methods, and administer them according to well-established routes and modes of administration.

3) Amount of guidance provided - Applicants submit that the teachings of the specification, e.g., as described herein, in combination with the knowledge and skill in the relevant art would have been sufficient to enable a skilled artisan to practice the methods of the amended claims without undue experimentation.

Applicants therefore submit that the factors cite by the Examiner are not sufficient to establish a *prima facie* case of non-enablement of the amended claims.

Even if the Examiner had established a *prima facie* case of non-enablement, Applicants submit that such a case is effectively rebutted by experimental evidence of making and using vault-like particles of the instant claims as taught in the specification. Applicants submit herewith under 37 C.F.R. § 1.132 the declaration of Leonard Rome, Ph.D., who is a co-inventor of the subject matter of the instant claims. The Declaration describes a series of experiments performed by or under the direct control of Dr. Rome, in which vault-like particles were made and used to deliver substances as set forth in the instant claims (Decl. at 4-5). The experiments were carried out by following the teachings of the specification, using known methods and the routing optimization of experimental conditions (*Id.* at 3). Moreover, the experiments were completed within several months of the filing date, indicating a lack of undue experimentation (*Id.*). The Declaration of Dr. Rome thus indicates that, even if the specification was *prima facie* non-enabled, the teachings of the specification were in fact sufficient to allow a skilled artisan to make and use the claimed invention.

In light of the above, Applicants submit that the instant specification, in combination with the knowledge and high level of skill in the art, would enable a skilled artisan to make and use the full scope of the *claimed* invention without undue experimentation. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

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**PATENT**

### **CONCLUSION**

Applicants have addressed all of the Examiner's concerns stated in the Office Action of January 10, 2008. Accordingly, Applicants respectfully submit that pending claims are now patentable and request a notice to that effect.

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